Is it worth collapsing a polymer chain? In vitro biocompatibility and in vivo distribution studies of Dextran based SCPNs and non-crosslinked polymer

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Introduction

SCPNs are soft nano-objects obtained by controlled compaction of a unique chain of the polymeric precursor. In spite of the progress in terms of synthesis and characterization and the promising scenery for future applications in biomedicine, there are no examples of SCPN-based nanomedicines at present.

Here, a validated *in vitro* model of the human airway epithelium and in vivo SPECT lung imaging were carried out to demonstrate the advantages of SCPN compared to the corresponding non-crosslinked polymer.

Results and Discussions

After demonstrating the cytocompatibility of both DXT-SCPNs and DXT, cellular uptake of both compounds was studied at 2 concentrations. Regardless of the concentration, DXT-SCPNs showed a faster internalization in both cell types. This effect was more evident in the case of BEAS2b cells, where only 1 hr was required for >90% of the cells incubated with the NPs at of 0.5 mg/mL to be SCPN-AF positive, while similar levels of DXT-AF were achieved after 16 hrs with the polymer. After In vivo administration, visual inspection of SPECT-CT images suggests that the residence time of SCPN-NODA-Ga nanoparticles and DXT-NODA-Ga polymer is longer than the residence time of control ^{67}Ga-Citrate. Animals sacrifice showed that 40 % of DXT-SCPN-NODA-Ga were cleared from the lung whereas the whole non-crosslinked DXT remained.TEER values of the cell monolayer were measured using MucilAir™ Pulmonary barrier to verify the barrier integrity in presence of DXT-SCPNs. It was found that TEER remained constant after exposure to DXT-SCPNs and therefore this system is not expected to alter the pulmonary epithelium.

Conclusions

Herein, we provide evidence of the better internalization of SCPNs by lung cells compared to the corresponding non-crosslinked polymer. The non-crosslinked polymer appeared to accumulate in rat lung whereas DXT-SCPN showed steady clearance, confirming the advantage of using SCPN technology.

Figures

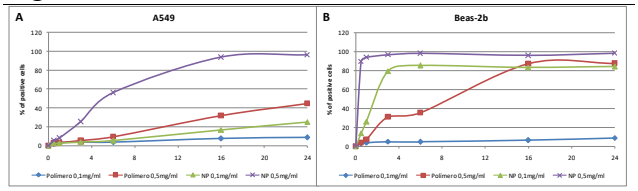

Figure 1. Percentage of SCPN-AF and DXT-AF positive cells after 24 hours of SCPN-AF incubation.

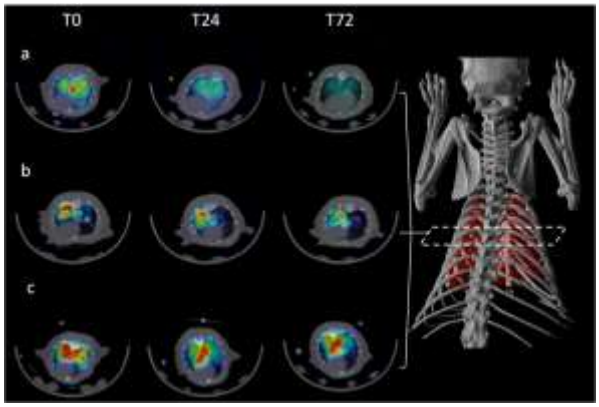

Figure 2. Left: SPECT-CT images obtained at 0, 24 and 72 hours after intratracheal nebulization of ^{67}Ga-Citrate (a), DXT-NODA-Ga (b), SCPN-NODA-Ga (c). Right: 3D-rendered CT image of the skeleton (grey tones) corregistered with a 3D-rendered image of the lungs (in red).